MU Covid Updates

Novavax Trial Information

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Health Care

Vaccine Development –
Vaccine Platforms

- Inactivated vaccines
  - Produced by growing SARS-CoV-2 in cell culture, then chemically inactivating it
  - Inactivated virus is combined with an alum or another adjuvant to stimulate an immune response
  - Target spike protein as well as other proteins
  - Several prototypes in late stage development
    - BBIBP-CorV (Sinopharm – China)
    - CoronaVac (Sinovac – China)

Vaccine Development –
Vaccine Platforms

- Live attenuated vaccines
  - Produced by developing genetically weakened versions of wild-type virus, which replicate in the recipient to generate an immune response but do not cause disease
  - Attenuation: modifying virus genetically OR growing it in adverse conditions, so virulence is lost but immunogenicity is maintained
  - A live attenuated SARS-CoV-2 vaccine would hopefully induce both humeral and cellular immunity to multiple components of the virus
  - Can also be administered intranasally, potentially inducing a mucosal immune response at the site of viral entry
  - Risks: reversion to or combination with wild-type virus
  - Several live attenuated SARS-CoV-2 vaccines in preclinical development, none have reached human trials

Vaccine Development –
Vaccine Platforms

- Vector vaccines
- Replication-incompetent vector vaccines
  - Engineered to NOT replicate in vivo, but to express viral protein which is the immune target
  - Most vaccines use an adenovirus vector, other viruses are also used
  - One drawback is that pre-existing immunity to the vector virus can reduce immunogenicity of the vaccine virus; to combat this, we can use viral vectors that are not familiar to humans (e.g. chimpanzee adenovirus) or human viral vectors that do not induce human immune response
  - Several in late stage development
    - ChAdOx1 nCoV-19/AZD1222 {AstraZeneca/University of Oxford)
    - AD26.COV2.S (Janssen)
    - Ad5-based COVID-19 Vaccine (CanSino Biologics, China)
    - Sputnik V (Gamaleya Institute, Russia)

Vaccine Development –
Vaccine Platforms

- Vector Vaccines, continued
- Replication-competent vector vaccines
  - Vectors are derived from attenuated or vaccine strains of viruses, resulting in a more robust immune response because they replicate in the recipient
  - Could be administered intranasally as well to induce mucosal immune response
  - Several are in early stage clinical trials
- Inactivated virus vector vaccines
  - Engineered to express target protein, but are inactivated
  - Safer, can be used in immunocompromised host
  - Still in preclinical development

Vaccine Development –
Vaccine Platforms

- DNA vaccines
  - Consist of plasmid DNA that contains mammalian expression promoters and the target gene, so the target protein is expressed in the vaccine recipient
  - Large quantities of stable DNA can be produce in E. coli, which is helpful for production
  - But, usually of low immunogenicity, and require specialized delivery devices, limiting their use
  - And, they must reach the nucleus to be transcribed to mRNA, so proteins can be generated to induce an immune response

Vaccine Development –
Vaccine Platforms

- RNA vaccines
  - The first SARS-CoV-2 vaccines to be produced
  - An entirely new vaccine approach
  - Once administered, the RNA is translated into the target protein which elicits an immune response
  - The mRNA remain in the cells' cytoplasm, but do not enter the nucleus and do not interact with or integrate into the recipient's DNA
  - Technology is new (for mass production, still a work in progress), and storage requirements can be complicated
  - Several are in late stage development and two are approved for use in US
    - BNT162b2 [*Pfizer*]
    - mRNA 1273 [*Moderna*]

Vaccine Development –
Vaccine Platforms

- Recombinant protein vaccines
  - Composed of viral proteins that have been expressed in one of various systems (e.g. insect cells, mammalian cells, yeast cells, plant cells)
  - Do not require replication of live virus
  - Production yield is variable depending on the ability to express spike protein
  - Recombinant SARS-CoV-2 vaccines in development include…
    - Recombinant spike protein vaccines
      - One in late stage development: NVX-CoV2372, by Novavax
    - Recombinant RBD (receptor binding domain) vaccines
    - Virus-like particle (VLP) vaccines

NVX-CoV2373 – Novavax Vaccine

- A recombinant protein nanoparticle vaccine composed of trimeric spike glycoproteins and a potent Matrix-M1 adjuvant
  - Targets spike protein antigen
- Phase I/II randomized, placebo-controlled trial of healthy individuals <60 years old showed high binding and neutralizing responses, comparable to those in convalescent plasma from patients who had been hospitalized with COVID-19
- Approximately 6% of participants experienced severe systemic effects (mainly fatigue, headache, myalgias, and/or malaise) following the second dose (see next slide)

ORIGINAL ARTICLE

Phase 1–2 Trial of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine

Cheryl Keech, M.D., Ph.D., Gary Albert, M.S., Iksung Cho, M.S., Andreana Robertson, M.S., Patricia Reed, B.S., Susan Neal, Joyce S. Plested, Ph.D., Mingzhu Zhu, Ph.D., Shane Cloney-Clark, B.S., Haixia Zhou, Ph.D., Gale Smith, Ph.D., Nita Patel, M.S., et al.

Novavax Vaccine Trial

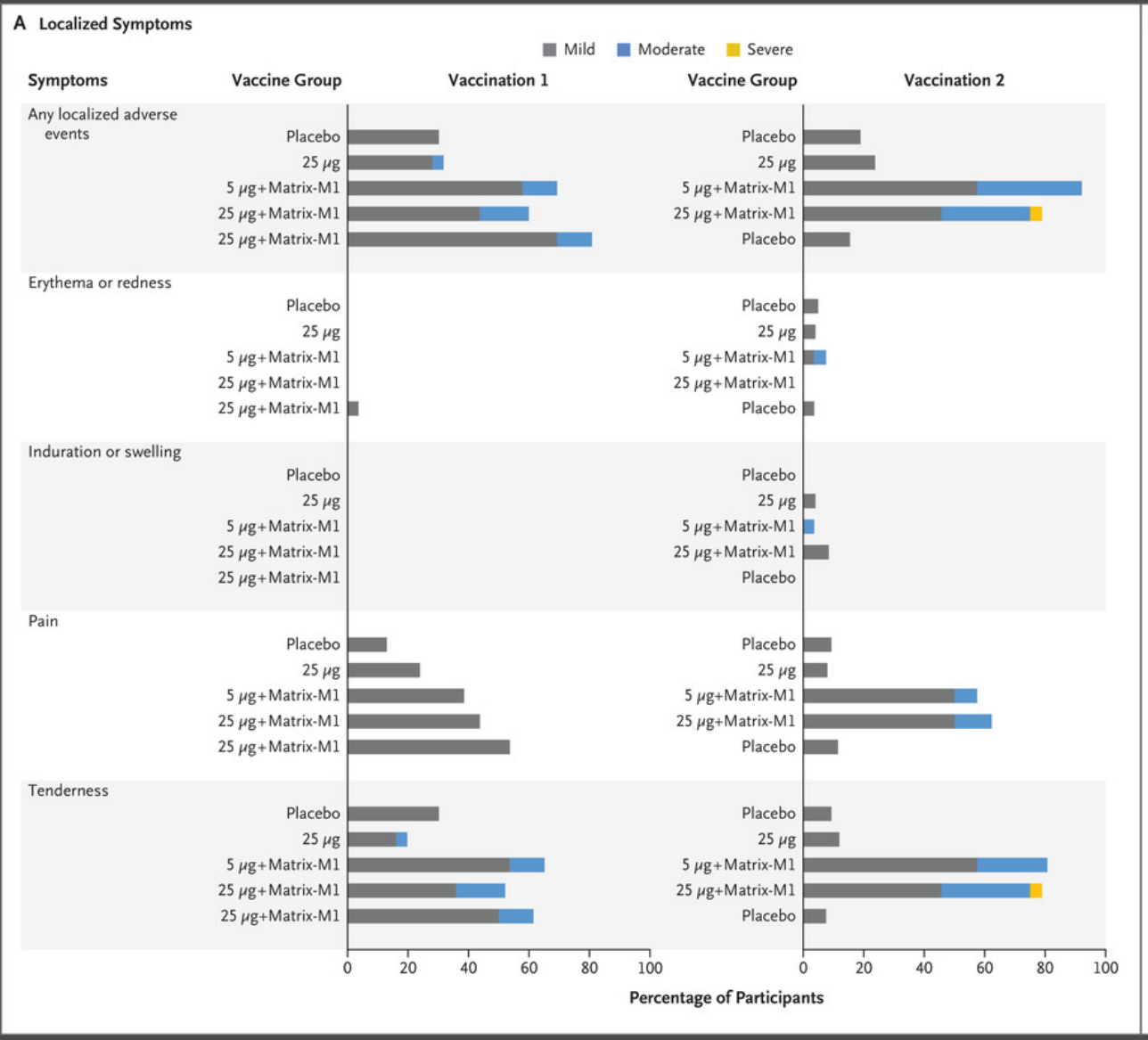
- MU HealthCare is participating in a phase 3 clinical trial to test the safety and efficacy of NVX-CoV2373 developed by Novavax
- Novavax is a late-stage biotechnology company that develops next-generation vaccines for serious infectious diseases
- Intramuscular injection, two doses given 21 days apart
  - Participants are randomized 2:1 to receive either vaccine or placebo
- We anticipate total enrollment of up to 30,000 participants in the US and Mexico

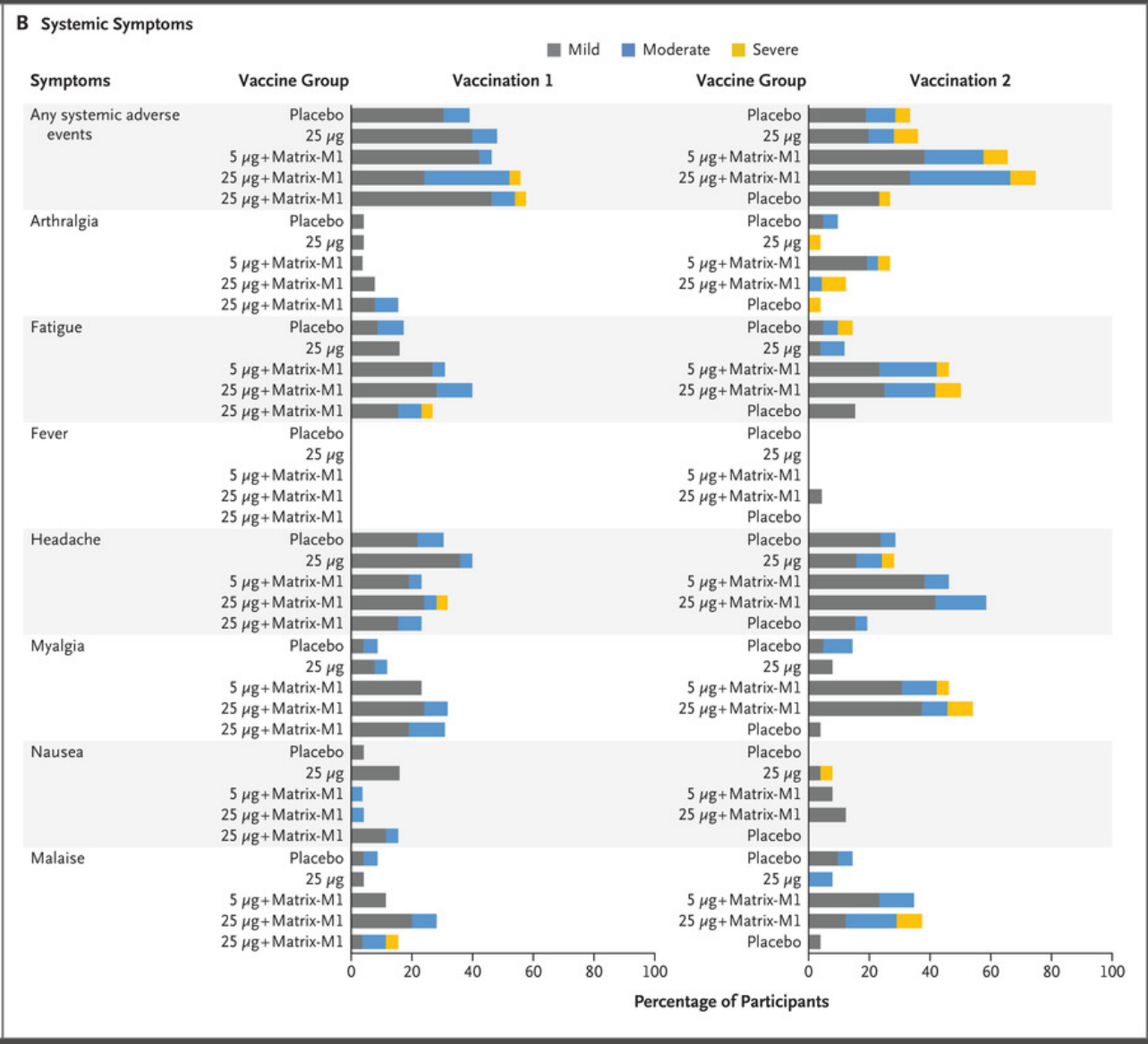
Novavax Vaccine Trial

- Participants must be 18 or older
- One potential benefit of this vaccine include less stringent storage requirements which may be useful in areas without access to specialized storage (i.e. ultra freezers)

NVX-CoV2373 – Novavax Vaccine

More localized and systemic symptoms after dose 2, and in higher dose groups





Novavax Vaccine Trial

- We were just green-lit as a site last week, so we are ramping up enrollment
- If you have patients, friends, family members who would be interested, please feel free to refer them to us for more information

nelsontb@health.missouri.edu

About This Study

COVID-19 has become a global health threat, and the need for a safe and effective vaccine is critical. There is currently no US Food and Drug Administration (FDA)-approved vaccine to prevent COVID-19.

This COVID-19 clinical trial is testing whether this vaccine will prevent COVID-19. It will compare this vaccine with a placebo, a substance that contains no active medication.

Participants who qualify for the study will receive:

- Study-related medical tests throughout the study
- The study vaccine or placebo
- Study-related monitoring of health and follow-up care

By participating in this study, you will make an important contribution to advance COVID-19 research. Speak with a study team member to learn more today!

Thank you for taking the time to consider joining this COVID-19 vaccine clinical trial.

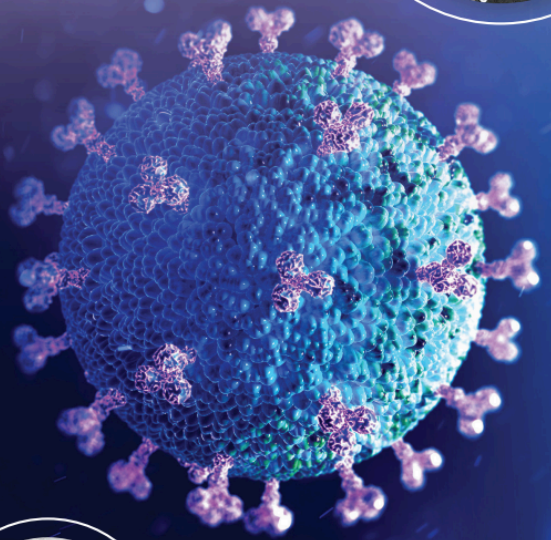
Contact us to learn more:

<Insert Site Contact Details>

NVX-020CTM_Participant Brochure_V1_27AUG2020

Join the Fight Against COVID-19

YOU CAN HELP WITH THIS VACCINE CLINICAL TRIAL



Who Can Participate

You may be eligible to participate in this COVID-19 vaccine clinical trial if you:

- Are an adult 18 years or older

We are specifically interested in those who:

- Represent a racial and ethnic group that has been greatly impacted by the pandemic (such as African American, Latinx, Native American, or Asian American)
- Have an underlying medical condition (such as diabetes or obesity)
- Have a high risk of exposure through work (such as first responder, healthcare professional, or delivery person)
- Live or work in an elder-care facility
- Are retired or active military

Other criteria will need to be met to confirm your eligibility for this study.

If you qualify and choose to join the study, you may be compensated for your participation.

What to Expect

Participation for this study is divided into 3 periods:

- **Screening:** The study team will determine if you are eligible to take part in the study
- **Vaccine:** All participants will get 2 injections of the study vaccine or placebo on the first day and again 3 weeks later
- **Follow-up:** The study team will monitor your health until 2 years after the last injection

You will be **randomly assigned** (by chance) to get either the study vaccine or placebo. Neither you nor the study doctor will know which group you are in or which injection you receive. Each participant will receive 2 injections.

Participants who receive the placebo vaccine may be eligible to receive the investigational vaccine after completion of the study.

Active Self-Monitoring

Participants will monitor their body temperature daily and look for symptoms of COVID-19 infection. Participants will report this information on an electronic questionnaire.

About Clinical Trials

A clinical trial, also called a clinical study, is carefully supervised research that is done before a study drug is approved and made available to the public.

- Clinical trials follow specific laws to protect the rights, safety, well-being, and confidentiality of study participants
- The results help government agencies like the US FDA determine if a product is safe and should be made available to the public
- Clinical trials are used to develop new prevention methods and medical treatments

Participating in a clinical trial is completely voluntary.

Taking part in the study will provide information about the study vaccine. If the results show that the study vaccine prevents COVID-19, this vaccine could become available for others, potentially protecting them from COVID-19 now and in the future.

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For more information

- clinicaltrials.gov
  - **A Study Looking at the Efficacy, Immune Response, and Safety of a COVID-19 Vaccine in Adults at Risk for SARS-CoV-2**

To enroll:

- https://www.muhealth.org/form/covid-19-vaccine-screening
- https://connect.trialscope.com/studies/6b7d56e0-2887-46d1-b639-1e6a5fb26b7d?pv=1

- If you (or your patients, family, friends) have questions or are interested in participating in our clinical trial at the University of Missouri please call 573-882-4894

Health Care

Thanks!

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